Perceived Symptoms of Hypoglycaemia in Elderly Type 2 Diabetic Patients Treated with Insulin

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Elderly insulin-treated diabetic patients have a high risk of severe hypoglycaemia, yet their hypoglycaemic symptom profile has attracted little research. In this study, the frequency and intensity of symptoms of hypoglycaemia were recorded using a validated questionnaire in 132 insulin-treated diabetic patients, aged 70 years or more. Principal components analysis (PCA) was used to discover the factorial structure of the symptoms. Lightheadedness and unsteadiness were prominent symptoms in the elderly patients. PCA suggested three separate groups of symptoms: (1) those related specifically to impairment of co-ordination and articulation; (2) more general neuroglycopenic symptoms, and (3) autonomic symptoms. The frequency and classification of hypoglycaemic symptoms in this elderly population is different from those seen in younger diabetic patients treated with insulin. Neurological symptoms of hypoglycaemia were more commonly reported and may be misinterpreted as features of cerebrovascular disease. Health professionals and carers involved in the treatment and education of diabetic patients should be aware of the age-specific differences in hypoglycaemic symptoms.

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Introduction

Using multivariate statistical methods, symptoms of hypoglycaemia in adults with Type 1 (insulin-depenent) diabetes mellitus have been classified into three distinct groups. Such methods have been used to categorize symptoms described by patients during experimentally induced acute hypoglycaemia[1] and in larger retrospective studies.[2] The symptoms groups are *neuroglycopenic* (confusion, drowsiness, odd behaviour, speech difficulty, and inco-ordination), *autonomic* (sweating, pounding heart, shaking, and hunger) and *general malaise* (nausea and headache),[2] and this has allowed the development and validation of a questionnaire to score hypoglycaemic symptoms (the 'Edinburgh Hypoglycaemia Scale'). This classification of symptoms is consistent with those derived from physiological studies.[3,4] A similar profile of hypoglycaemic symptoms occurs in patients with Type 2 (non-insulin-dependent) diabetes who are receiving treatment with insulin.[5]

The hypoglycaemic symptoms experienced by children with Type 1 diabetes differ from those of adults, with behavioural disturbance being a prominent feature which is evident to their parents.[6] The nature and clustering of hypoglycaemic symptoms may therefore be age-related. Elderly diabetic patients treated with insulin are also at high risk of developing severe hypoglycaemia,[7] and it has been assumed previously that their hypoglycaemic symptom profile is the same as that of younger adults with diabetes.[8,9]

In the present study, the statistical technique of principal components analysis (PCA)[10] has been applied to investigate the groupings of hypoglycaemic symptoms reported by a sample of elderly adults with insulin-treated Type 2 diabetes.

Patients and Methods

One hundred and thirty-two patients with Type 2 diabetes mellitus, aged 70 years or more, who were receiving treatment with insulin, were selected consecutively during routine attendance at diabetic outpatient clinics. Of these, 102 had experienced hypoglycaemia within the preceding 2 months and were asked to record retrospectively their subjective experience of the presence of 22 symptoms of hypoglycaemia during a 'typical' hypoglycaemic episode by estimating their intensity (on a 7-point scale) using a standard questionnaire. The symptoms used were those reported in a previous study of hypoglycaemia in younger Type 2 diabetic patients treated with insulin.[5] In addition, 4 symptoms (dizziness, lightheadedness, shivering, and double vision) reported

Abbreviations: PCA principal component analysis

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in a previous survey of hypoglycaemia in the elderly[8] or noted in clinical experience were included, along with one event (convulsions) to attempt to identify severe hypoglycaemia in the absence of other warning symptoms. Two dummy symptoms unrelated to hypoglycaemia (itching and hiccups) were included.

As this was a retrospective study, biochemical verification of all hypoglycaemic episodes was not possible. However symptoms were only attributed to hypoglycaemia if they settled following the administration of oral carbohydrate, parenteral glucose or glucagon. In addition, corroboratory evidence on the frequency and symptom profile of hypoglycaemic episodes was provided by relatives completing a similar questionnaire if possible.

The 102 patients (56 females) were aged 74.5 ± 0.7 years (mean $\pm$ SD), with known duration of diabetes of 15.5 ± 3.5 years, duration of insulin treatment for 8.8 ± 2.9 years, and had a mean total glycated haemoglobin (HbA_1) over the preceding 3 years of 11.7 ± 2.5 % (non-diabetic range 5–8 %, gel electrophoresis). None of the subjects had a blood glucose of less than 4.0 mmol l^{-1} at the time of completing the questionnaire. With respect to macrovascular complications of diabetes, 6.9 % of the patients had a history or clinical evidence of cerebrovascular disease, 15.3 % had ischaemic heart disease, and 10.4 % had peripheral vascular disease.

Patients and their relatives ratings of the frequency with which hypoglycaemic symptoms occurred were compared using Spearman's rank correlation. Principal components analysis (PCA) with varimax (orthogonal) rotation were used to investigate the latent structure within the reported hypoglycaemic symptoms.[10] PCA is a multivariate statistical technique which affords a valid method for 'data reduction'. It enables a large set of variables to be reduced to a smaller number of latent variables (or factors), which comprise subgroups of measured variables that have high intercorrelations. The criterion for factor extraction was closeness to simple structure, which is said to be present when most rotated factor loadings are either very high or very low, indicating the distinctiveness of the factors. Those symptoms for which more than 80 % of responses were at an intensity of one (i.e. not present) were considered to show insufficient variance, and were omitted from PCA.

Results

The most frequently reported and intense hypoglycaemic symptoms were unsteadiness, lighheadedness, poor concentration, trembling, and sweating (Table 1). No patients reported dummy symptoms. The median number of hypoglycaemic episodes in the previous year was 6 (range 2–24). Twenty-seven relatives completed questionnaires and a similar pattern for the frequency of hypoglycaemic symptoms was reported by patients and their relatives (Rs 0.58, $p < 0.05$). Subgroup analyses of those patients with known cerebrovascular disease or any form of macrovascular disease did not show any major differences in the spectrum of hypoglycaemic symptoms experienced.

The results of PCA are shown in Table 1. The first unrotated principal component (FPC) indicates whether or not there is a general factor underlying most of the measured variables. Most of the symptoms included in the questionnaire loaded moderately or highly on the FPC, confirming that there is a 'general hypoglycaemia factor' in the elderly. A three factor solution showed the best approximation to simple structure. Rotated factor 1 contained general neuroglycopenic symptoms (e.g. weakness, drowsiness, confusion, and poor concentration); factor 2 comprised autonomic symptoms (e.g. sweating, shivering, and pounding heart); while those with the highest loading on factor 3 were neuroglycopenic symptoms specifically related to co-ordination and articulation (e.g. double vision, slurred speech, and poor co-ordination).

Discussion

This study describes the frequency and classification of hypoglycaemic symptoms in elderly diabetic patients treated with insulin. This was a retrospective study, and therefore subject to inaccurate recall, especially in elderly subjects, but steps were taken to minimize this by including only patients who had recent and regular hypoglycaemia; asking patients to report their experiences of a 'typical' hypoglycaemic episode; and, where possible, obtaining corroboration from a relative. Inevitably some episodes attributed to hypoglycaemia may have had other causes, and confirmatory prospective studies correlating symptoms with biochemical evidence of hypoglycaemia are required as a follow-on to the current study.

In contrast to younger adults with Type 1 diabetes, some of the most prominent symptoms of hypoglycaemia reported by elderly insulin-treated Type 2 diabetic patients in the present study were not 'classic' hypoglycaemia symptoms (e.g. lightheadedness and unsteadiness) and could potentially be incorrectly attributed by observers to other causes such as cerebrovascular disease (e.g. transient ischaemic attacks). Diminished intensity of hypoglycaemic symptoms, fewer individual symptoms and attenuated counterregulatory hormonal responses have been observed in elderly non-diabetic subjects,[11–14] with more pronounced abnormalities being demonstrated in patients with Type 2 diabetes.[15] In the present study the mean reported intensities of hypoglycaemic symptoms were generally low. It should be noted that none of the patients were taking medication which may have affected responses to hypoglycaemia, such as non-cardioselective beta blockers. A previous study has suggested that autonomic symptoms during experimental hypoglycaemia are attenuated in elderly diabetic patients,[15] but a selective reduction in autonomic symptoms was not apparent in the present study. This may reflect reduced symptom intensity, methodological

Table 1. Frequency and intensity of hypoglycaemic symptoms in elderly Type 2 diabetic patients treated with insulin, and the results of principal components analysis

Symptom	Frequency (%)	Mean intensity[a]	FPC[b,c,d]	Factors		
				1	2	3
Poor concentration	68.7	2.1	**0.38**	**0.50**	0.09	0.19
Headache	10.0	1.3	–	–	–	–
Nausea	6.2	1.3	–	–	–	–
Sweating	75.0	3.3	**0.60**	0.19	**0.70**	–0.10
Confusion	60.0	2.6	0.27	**0.51**	–0.06	0.12
Trembling	71.2	3.1	**0.48**	0.09	**0.73**	0.02
Drowsiness	53.8	2.1	**0.50**	**0.63**	0.17	0.08
Tingling of lips	1.2	1.0	–	–	–	–
Dizziness	40.0	1.8	**0.33**	**0.44**	0.09	–0.08
Anxiety	26.3	1.5	**0.34**	–0.19	**0.35**	–0.22
Pounding heart	21.1	1.4	**0.46**	–0.29	**0.56**	–0.03
Shivering	35.0	1.6	**0.34**	0.09	**0.57**	–0.04
Weakness	65.4	2.7	**0.51**	**0.76**	0.05	0.01
Hunger	5.0	1.1	–	–	–	–
Blurred vision	46.2	2.3	0.20	0.12	–0.08	**0.46**
Double vision	20.4	1.5	0.29	–0.02	0.01	**0.69**
Convulsions	3.7	1.2	–	–	–	–
Odd behaviour	25.0	1.5	0.15	0.03	0.08	0.04
Slurred speech	25.1	2.0	**0.58**	–0.15	0.07	**0.79**
Poor co-ordination	60.0	2.8	**0.67**	**0.43**	–0.06	**0.66**
Unsteadiness	68.7	3.3	**0.69**	**0.41**	–0.01	**0.66**
Lightheadedness	68.7	3.1	**0.34**	**0.47**	–0.18	**0.33**

[a]Symptoms graded in increasing prominence on a scale from 1 to 7.
[b]First Principal Component.
[c]Symptoms where > 80 % of responses had intensity = 1 were omitted from PCA.
[d]Rotated factor loadings of 0.3 or grater indicate high intercorrelation and are shown in bold.

differences in the nature of the symptom questionnaire used or a small sample size,[15] but, in particular, experimentally induced hypoglycaemia may result in a different symptom profile to that experienced by ambulant patients in everyday life.

In the present study, PCA revealed a 3-factor grouping of hypoglycaemic symptoms in elderly diabetic patients. As in younger adults with Type 1 diabetes,[1,2] broad neuroglycopenic and autonomic factors were found in the present study. However, in contrast to younger diabetic adults, a general malaise factor did not emerge clearly, with older patients rarely reporting headache or nausea. The third factor comprised specific neuroglycopenic symptoms relating to co-ordination and articulation. This suggests that some areas of the ageing brain may be more susceptible to the effects of neuroglycopenia, possibly exaggerating the effects of the ageing process. Preliminary MRI studies of adult patients with a long duration of Type 1 diabetes have shown an increased frequency of cerebral atrophy and other changes suggestive of premature ageing.[16] Co-existence of cerebrovascular disease may also be relevant, and although no difference in the spectrum of symptoms experienced by those with known cerebrovascular disease was observed in the current study, it is likely that this population had a high frequency of undiagnosed cerebrovascular atherosclerosis. Alterations in regional cerebral blood flow during hypoglycaemia may also be important. Both regional hyperperfusion and hypoperfusion of the brain have been reported under conditions of euglycaemia in Type 1 diabetic patients, with more marked abnormalities being found in patients who had a history of recurrent severe hypoglycaemia.[17,18] Changes in regional cerebral blood flow have also been observed during acute hypoglycaemia in non-diabetic subjects.[19]

In summary, the frequency and grouping of hypoglycaemic symptoms in elderly insulin-treated diabetic patients are different from those reported in previous studies of younger adults and children.[1,2,5,6] Health professionals and carers involved in the treatment and education of diabetic patients should be aware of the age-specific differences in the symptoms of hypoglycaemia, and be able to recognize features of hypoglycaemia in the elderly patient treated with insulin. This age group may resemble the very young, in that their symptoms differ from those described classically in adults and they are much more dependent on carers to identify and treat hypoglycaemia. It is important that symptoms of hypoglycaemia in the elderly, especially those related to psycho- motor co-ordination, are not spuriously attributed to other causes such as cerebrovascular disease.

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